the absorbent power of the fundus seems to be even lower than that of the entire stomach.

The power of absorption in the œsophagus is somewhat better than in the stomach, but is still considerably inferior to the absorption within the other parts of the alimentary canal.

The power of absorption in the other three parts of the canal—*i. e.*, the small intestines, colon, and rectum—seems to be equal. The differences which were observed are too small and the method not exact enough to justify the assumption of an actual difference in the absorbing power of these parts. However, these experiments brought out the following remarkable facts: that the isolated rectum absorbs at least as well as the small intestines; that in some experiments the effects appeared earlier when the rectum was isolated than when it had free connection with the balance of the gut; that from no part of the canal were such short intervals between the injection of the strychnine and the appearance of the tetanus observed as were frequently seen when it was injected into the rectum—in the latter case the interval was sometimes only two or three minutes; finally, impaction of the rectum proved to be no hinderance to the prompt absorption of the poison therefrom.

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A CRITICAL SUMMARY OF THE LITERATURE

ON

SPLENIC PSEUDOLEUKÆMIA (ANÆMIA SPLENICA; SPLENOMEGALIE PRIMITIVE).[1]

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History of the Disease. The history of splenic pseudoleukæmia is inseparably connected with that of the diseases to which it is closely allied—namely, leukæmia and the other forms of pseudoleukæmia. Its study, therefore, may well trace the development of our knowledge of those diseases as a class. The attention of the medical profession was early directed to a complexus of symptoms characterized by enlargement of the spleen, pallor, hemorrhages, œdema, and grave cachexia. Hippocrates wrote on the association of splenic tumor with dysentery, hemorrhage, scorbutus, and miasmatic diseases. Galen described hypertrophy of the spleen in protracted autumnal fever and other cachectic states. Malpighi, Morgagni and others observed splenic and lymphatic enlargement associated with pallor, hemorrhage, and emaciation, which progressed to a fatal termination. Nivet[1] mentions scorbutus, rhachitis, and scrofula among the many causes of splenic enlargement. In some of the cases of splenic hypertrophy reported by him under the heading of rhachitis and scrofula, extensive glandular enlargement and grave cachexia developed during the course of the disorders. There is much in the literature of the older writers to indicate that they were quite familiar with hypertrophy of the spleen in miasmatic disease, and that they also had noted the condition in various other affections, such as scrofula, continued fevers, syphilis, and liver disease. Now and then one also finds record of cases in which, without apparent cause, the spleen enlarged, hemorrhages and cachexia supervened, and death followed. No particular types of disease of this nature were well recognized, however, until, in 1832, Hodgkin wrote his now well-known article on "Some Morbid Appearances of the Absorbent Glands and Spleen."[2] He reported a number of cases which showed an increase in the size of the lymph-glands and spleen, followed by emaciation, ascites, pallor, œdema, and death. The blood was not examined in any of the cases, and the report in many instances is meagre. One is able to discern, however, that undoubtedly the author's cases included carcinoma, tuberculosis, sepsis, and probably other morbid conditions. Nevertheless, it was the first worthy attempt to group this class of affections. In October, 1845, Bennet published the report of a case of hypertrophy of the spleen in which the blood of the patient contained a great number of white corpuscles resembling pus-cells. In November of the same year Virchow reported a similar case, and correctly attributed the large increase in the white cells to an augmentation of the white blood-corpuscles. He believed that the great increase in the leucocytes was due to the hypertrophy of the spleen. Subsequently, he evolved the doctrine of the disease, leukæmia, which he described as an affection characterized by cachexia, enlargement of the spleen and lymph-glands, and an augmentation in the number of white blood-corpuscles. Other histological changes of the disease described by him were cellular hyperplasia of the lymph-glands and spleen and infiltration of lymph-cells in the tissue of the liver, lungs, kidneys, and intestinal tract. Virchow recognized a lymphatic and a splenic form of leukæmia. In the year 1868 the work of Neumann and Bizzozero, on the hæmatopoietic function of the medulla of bone, gave rise to a new field of clinical observation, and soon a sufficient number of cases of leukæmia was recognized in which profound changes in the medullary substance of the bone were present to warrant a third subdivision of the disease—namely, myelogenic leukæmia. Shortly after Virchow's description of leukæmia, Bonfils, Trousseau, Wunderlich, Wilkes and others observed cases which presented extraordinary swelling of lymph-glands and spleen and many of the clinical features of leukæmia. It was noted, however, that the number of white blood-corpuscles was not increased. In order to distinguish these cases from leukæmia, Trousseau proposed the name *adenia*, by which the French still recognize the disease. Wilkes added that of *anæmia lymphatica*, or *Hodgkin's disease*. Wunderlich described it as *progressive glandular hypertrophy;* Virchow, as *lymphosarcoma;* Billroth, as *malignant lymphoma*, and Cohnheim, as *pseudoleukæmia*. Aside from the marked enlargement of the lymph-glands and spleen, the disease was characterized by pallor, hydrops, and a tendency to hemorrhages, cachexia, final marasmus, and death. The cases did not include similar clinical manifestations due to malaria, syphilis or any other apparent cause. The essential feature which distinguished the affection from leukæmia was the absence of an increase in the leucocytes. In many cases the lymph-glands only were enlarged; in other cases both the spleen and lymph-glands showed marked increase in size. To the first class of cases the older writers applied the terms *adenia, anæmia*, and *pseudoleukæmia lymphatica*. To the second class were applied the terms *adenia, anæmia*, and *pseudoleukæmia splenolymphatica*. More recently a relatively small number of cases have been reported, belonging to this class of diseases, in which the lymph-glands were unaffected, while the spleen was greatly hypertrophied. These cases present a most striking analogy to splenic leukæmia, the essential difference being in the alterations in the blood. The number of cases thus far recognized clinically does not exceed twenty-five, and the number of autopsies is still much smaller. The uniformity of the clinical and pathological features of the disease, however, establish the affection as a distinct morbid entity, which is, in reality, a splenic form of pseudoleukæmia. In 1856, Woillez described the first undoubted case of this disease under the title "Observations d'hyp. de la rate" (*Union Medicale*). His report referred to a man, forty years of age, who was taken sick without apparent cause. The disease was characterized by anæmia and a rapidly progressive course, which terminated in death. There was no increase in the number of leucocytes; the spleen measured 26 x 12 cm. Two enlarged glands were found in the and pathological features have been described under various names. Debove and Bruhl applied the term splenomegalie primitive; Eichhorst, splenic pseudoleukæmia; Gaucher, idiopathic hypertrophy of the spleen without leucocythæmia. (For reports of other cases, see references.) The manifold nomenclature arising in part from the different theories held by the different authors regarding the nature of the disease gives rise to a certain amount of confusion concerning the affection. At best, the terms leukæmia, pseudoleukæmia, and splenic anæmia simply designate a certain grouping of clinical manifestations and pathological changes.

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[1] For the author's report of a case, see The American Journal of the Medical Sciences, October, 1899, vol. cxviii., No. 330, p. 428.

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[1] Archives Generales de Medicine, 1838.

[2] Medico-Chirurgical Transactions.

If the ordinary forms of Hodgkin's disease were described as anæmia lymphatica and anæmia splenolymphatica it would be consistent to apply the term anæmia splenica to the rare cases under consideration. However, since the term pseudoleukæmia is more often applied to such conditions, I believe the appropriate name for this form of the disease is splenic pseudoleukæmia.

ETIOLOGY. The etiology of splenic pseudoleukæmia is unknown. The disease does not appear to bear any direct relation to malaria, syphilis, tuberculosis, or alcoholism. It seems to arise independent of all constitutional disorders. The cultures obtained from the spleen in my case, both ante-mortem and post-mortem, contained no organism that could be regarded as specific, and the spleens of animals injected with blood from the spleen of the patient showed no changes. The microscopical examination of the spleen and other organs revealed no micro-organisms. In 1894, Sciolla obtained negative results from cultures made from the spleen ante-mortem. The negative results in the two cases mentioned do not, of course, exclude micro-organisms as a cause of the disease. However, certain features in connection with the disorder render it very improbable that a specific micro-organism is the etiological factor. The disease is extremely rare, and has never occurred endemically or epidemically. Isolated cases have appeared in different parts of the world. More cases have been recognized in Italy than in any other section. There appears to be no special predisposing cause of the disease.

PATHOLOGICAL ANATOMY. I find record of only about ten post-mortems in which it is reasonably certain that splenic pseudoleukæmia was the cause of death. As a rule, the cadaver presents a high grade of emaciation. In some cases the subcutaneous fat has been well retained. The skin and conjunctivæ are subicteric, and punctiform hemorrhages may be visible in different parts of the body. Usually the subcutaneous connective tissue of the dependent parts is infiltrated with serum, and œdema of the extremities is often present. Visible external glandular enlargement is seldom found, yet it is not rare to be able to palpate a few glands, the size of a bean or a hazel-nut, in the inguinal or axillary regions. The abdomen usually contains a variable quantity of ascitic fluid. Ecchymoses may be present beneath all the serous surfaces. The pericardial sac often contains a serous fluid. The heart is generally slightly dilated, and frequently presents signs of granular and fatty degeneration of its muscle, such as is usually found in severe anæmia. The pleural cavities often contain fluid, and when the spleen is extremely large, compression of the left lung may give rise to atalectasis of its lower lobe. In a few cases a real pleurisy has been present on the left side. Although nausea, vomiting, and diarrhœa may be prominent symptoms throughout the course of the disease, the gastro-intestinal tract does not present serious alterations. The glands at the base of the tongue have been found somewhat enlarged. Not infrequently Peyer's patches and the solitary follicles show slight hyperplasia. The liver is usually enlarged. In my case it weighed 2800 grammes, which exceeds by far the usual weight recorded in this affection. Its surface is smooth, the edges round, and the organ presents, as a rule, no visible signs of cirrhosis. On section, the organ is uniform in firmness, cuts easily, and its consistency is not apparently increased. Histology of the liver: The liver shows slight increase in its interlobular connective tissue. Infiltration of round cells is observed about the portal vessels and between the liver lobules. In a case reported by Banti there was considerable increase in the connective tissue, which he described as an interstitial perilobular hepatitis. The liver cells may be normal. Here and there, where there is considerable proliferation of connective tissue, the hepatic cells may be atrophic. The spleen is always increased in size, and often fills the greater part of the left half of the abdominal cavity. The normal size of the spleen is 12 x 8 x 3 cm.; its normal weight is 200 grammes. In my case it measured 31 x 16 x 9.5 cm. and weighed 2350 grammes. The normal shape and outline of the organ is preserved. Its surface is usually smooth, although in some cases areas of peritoneal thickening resulting from perisplenitis are present. Rarely peritoneal adhesions have been recorded. The organ is firm. In a case reported by Banti there was a visible increase in the connective tissue. Small white areas, about the size of a pea, were noted by him, which proved to be made up of increased connective tissue. In my case there was no macroscopic increase in the connective tissue. The Malpighian corpuscles were not visible. Histology: The Malpighian corpuscles are usually not markedly altered. Banti records considerable sclerosis of these bodies in one of his cases. He summarized his findings in the spleen as (1) atrophy and sclerosis of the Malpighian corpuscles; (2) the substitution of an irregular and fibrous reticulum for the normal fine reticular substance of the splenic pulp. The following quotation is from a case reported by West: "The spleen showed slight increase in the trabecular tissue—*i. e.*, slight fibrosis. Malpighian corpuscles are much diminished in size and badly developed. Iron reaction negative." For the changes in the spleen in my case the reader is referred to the histology given in the report. The kidneys are anæmic. The epithelium of the tubules may show signs of granulo-fatty degeneration. A real nephritis, however, is not present. The pancreas and adrenals are negative. The lymphatic glands are usually not enlarged. In some cases, however, isolated glands, or small groups of glands, especially in the retroperitoneal region, have shown slight enlargement. They are grayish and somewhat red, and firm in consistency. On section they show no softening, and the microscope reveals hyperplasia of both the principal elements. The mesenteric glands may show similar changes. The medulla of the bone often presents an appearance closely resembling that found in primary pernicious anæmia. In one of Banti's cases he notes that the medulla in the long bones was, as a rule, fatty; but that in both femora a fœtal condition of the marrow was present. In my case the compact tissue of all the bones was very much reduced, producing a considerable degree of brittleness. The sternum could easily be broken with the fingers. Throughout the length of the femur, tibia, and humerus the normal fat was replaced by dark red marrow. Indeed, red atrophy of the marrow was distinctly present in every bone examined, including, beside those mentioned, the ribs, clavicle, skull, vertebræ, and small bones of the feet. The blood changes found in the disease are described under the symptomatology.

SYMPTOMATOLOGY. The following description of symptoms is based on those present in my case, supplemented by a study of the cases most carefully reported. The manner of onset varies; as a rule, however, the disease begins very insidiously, so that it is often difficult to establish the period at which the first manifestations of the affection appeared. In many cases the first symptoms noted are cardiac palpitation on exertion, accompanied by a feeling of unusual muscular fatigue. Headache and slight pallor of the mucous membranes may be present. Early in the disease the appetite and digestion are usually good and the bowels regular. After a period varying from a few weeks to two or three months the attention of the patient is attracted to the existence of a tumor in the left hypochondriac region. The tumor is seldom painful, and disturbs the patient chiefly by a sense of weight and tension in that region. In some cases, as in my own, a tumor in the left hypochondriac region is the first symptom noted by the patient. Shortly after this discovery, owing in part, no doubt, to the mental concern of the patient in regard to his disorder, a feeling of weakness on muscular exertion is experienced. Following this may appear nausea and vomiting and at times persistent diarrhœa. Dyspnœa and cardiac palpitation on exertion may be rather prominent features. Now and then dizziness and headache may be experienced. Epistaxis is a common early symptom.

In other cases a tumor may appear in the left hypochondriac region, which may increase in size for nearly a year without any disturbance in the general health or even local disturbance, aside from a feeling of weight or tension in the part. After a variable time—seldom longer than a year—the symptoms of anæmia and general disorder in organic function supervene. In rare cases, as in one reported by Debove, the local phenomena referable to the spleen may be very distressing. Pain, paroxysmal in character, simulating hepatic colic, with attacks of nausea and vomiting, may accompany the gradual loss of muscular power and signs of anæmia. Examination of the patient may then reveal the signs of marked anæmia and a palpable tumor in the left hypochondriac region. It matters not what the mode of onset is; after the disease has developed the clinical picture will present the same essential features: (1) Hypertrophy of the spleen; (2) absence of marked lymphatic enlargement; (3) anæmia progressing toward a cachectic state. At this time the symptoms are all very pronounced, with the exception of pain, which may be only slight or entirely absent throughout the whole course of the affection. Debility is great; œdema appears, at first transitory in character, involving the ankles and wrists. A vespertine fever, preceded by chilly sensations, may be present. Gastro-intestinal disturbances, manifested in anorexia, indigestion, and diarrhœa, are present in varying degrees of intensity. Finally, within a period of a few weeks or months, the cachexia of anæmia becomes pronounced. Emaciation gradually increases. The skin and conjunctivæ become subicteric; pallor peculiar to profound anæmia appears. Muscular weakness confines the patient to his room or bed. Œdema becomes permanent and is associated with ascites and hydrothorax. Petechial hemorrhages on the extremities and in the mucous membranes evidence the high grade of malnutrition of the capillary walls. Persistent and often incoercible diarrhœa exhausts the patient, and involuntary evacuation of the bowels may announce the approach of dissolution. At the beginning of the cachectic stage the blood examination usually shows a grade of anæmia which approximates very closely the findings in chlorosis. As the cachexia increases the number of red blood-corpuscles, as a rule, diminishes, until finally, as in my case, less than one million per cubic millimetre may be registered, with hæmoglobin so slight in amount as to preclude the possibility of accurate estimation. At no time, however, is there a leucocytosis presenting the characteristics found in leukæmia. From a scientific as well as therapeutic stand-point it is extremely interesting to note that so far as may be gleaned from the histories of the cases, the splenic hypertrophy has preceded or at least has developed contemporaneously with the appearance of the anæmia. In no case belonging properly to this type of disease, so far as I have been able to discern, has the splenic hypertrophy followed the appearance of the anæmia. In the majority of cases the patient has not consulted the physician until his attention has been attracted to the tumor in the side. In my case the patient, naturally a quick observer, was not conscious of any unusual physical manifestation until he discovered a tumor a few inches below the costal arch in the left hypochondriac region. The fact that splenic hypertrophy is apparently the primary condition has an important bearing on the treatment of the disease. It also contributes much to the nature of this type as well as the other forms of pseudoleukæmia. As a rule, in the progress of the disease the size of the spleen bears a direct relation to the grade of anæmia. However, there are exceptions, in which the spleen is enormously enlarged before anæmia is pronounced. In still other cases anæmia may be profound when the splenic tumor is of moderate size. After cachexia develops the disease is usually rather rapidly progressive, and death is due to complications, or it follows a period of extreme marasmus. The disease may be divided into three stages. The first stage includes an indefinite period, during which the spleen begins to enlarge. The second stage may conveniently be said to include that period during which the symptoms of anæmia develop, accompanied, as a rule, by gastro-intestinal disturbances and general asthenia. The third stage is that of cachexia. This stage is usually ushered in with œdema, followed by a somewhat regularly progressive aggravation of all the symptoms of the previous stages, and finally terminates in extreme marasmus and death.

SPECIAL SYMPTOMS. *Splenic Hypertrophy.* So far as is known, all the disorders of the spleen that are of clinical importance are accompanied by its enlargement. Splenic pseudoleukæmia presents as one of its essential features an enlargement of the spleen. The enlargement is uniform, constituting a true hypertrophy in a clinical sense. Its size varies with the stage of development of the disease, and is not the same in all cases. The spleen enlarges gradually, and is not subject to marked fluctuations in size. Owing to the fact that the first stage of splenic enlargement is seldom observed, it is impossible to estimate its rapidity of growth from the beginning. In my case, after the spleen was first palpable, it gradually enlarged until its lower border reached a point two fingers'-breadth above the pubic bone, and its inner border extended beyond the median line, the patient in the upright position. In this case it appears that the enlargement was exceptionally great. Usually the organ extends no further than one or two hands'-breadth below the costal arch. Its outline is symmetrical. As a rule, no irregularities are to be felt, either on its margin or surface. Its consistency is firm. The splenic notch occupies its usual position. The organ is respiratory, movable in a diagonal direction, peculiar to splenic enlargement, and permits of lateral movement. Pain on pressure may or may not be present. In my case a loud souffle was to be heard all over the enlarged organ. In some cases friction rubs, due to perisplenitis, have been heard. A perisplenitis may result in local thickenings that may be felt as irregularities on the surface of the organ. When the enlargement is marked the left half of the abdomen is more prominent than the right, and the region of the left costal arch appears bulging. In my case, just previous to death and at the time of great diarrhœa and involuntary discharges, the spleen was reduced fully two inches in its various diameters. The enlargement of the spleen may be unaccompanied by pain. In the majority of cases an uncomfortable sensation of weight and fulness in the left hypochondriac region leads to the discovery by the patient of the tumor. In rare cases neuralgic pains or paroxysms resembling hepatic colic, accompanied by obstinate vomiting, appear as early manifestations of the disease. At times the pain may be so intense as to demand radical means for its relief. The explanation of the pain is not always apparent. A perisplenitis is often found, but pain has been a marked feature when such a condition was not present. In all cases when pain exists it is increased by pressure.

Lymph-glands. The lymph-glands may remain normal in size throughout the course of the disease. It is not uncommon, however, for the post-mortem to reveal enlargement of the retroperitoneal and bronchial glands, either isolated or in groups. The glandular hypertrophy, if present, is always moderate. In a few cases, after splenic hypertrophy had existed for a long time and the symptoms of the disease were well developed, small kernels have appeared in the axillary and inguinal regions. The glands at the base of the tongue and the tonsils have been found enlarged.

Liver. The liver is nearly always considerably enlarged; its surface and outline are regular, its consistency firm, and its lower border sharp. Perihepatitis may occur.

Anæmia. Anæmia is one of the characteristic features of the disease. So far it has not been recorded in any case that the signs of anæmia preceded the development of splenic hypertrophy. The symptoms of anæmia develop gradually during the second stage of the affection, until that state of profound alteration of general nutrition is reached which is clinically designated by the term cachexia. During this stage dizziness, tendency to syncope, headache, dyspnœa on exertion, and cardiac palpitation are present in variable degrees of intensity. Pallor of the mucous membranes gradually develops. Hæmic heart-murmurs may be heard. The skin assumes a hue peculiar to anæmia—pallid at first and later on of a yellowish tinge. The conjunctivæ become slightly subicteric. Epistaxis, such as may occur in anæmia from any cause, is often a frequent and early symptom. The hemorrhage is seldom profuse. The advent of cachexia is characterized by a tendency to œdema and effusion into serous cavities, marked asthenia, hemorrhages, fever, and an aggravation of all the pre-existing symptoms. The mucous membranes become exceedingly pale. The carotids pulsate visibly. Capillary pulse may be present. A venous hum is often noted. The patient gradually emaciates. Persistent diarrhœa often supervenes in the later stages, and anæmia progresses to the highest degree. A period of extreme marasmus finally terminates in death.

Cachexia. The cachexia of splenic pseudoleukæmia does not differ from the cachexia of carcinoma, tuberculosis, or any other profound disturbance of nutrition. Although epistaxis is frequently an early symptom, hemorrhage from other organs than the nose seldom takes place until cachexia develops. During this stage hæmatemesis, hæmoptysis, melænæ, and hæmaturia have been observed, and petechiæ of the skin and mucous membranes is common. Retinal hemorrhages are to be expected.

Fever. Fever may be present during the early stage of the affection. It is a variable symptom, and may be absent for weeks at a time, and then irregular pyrexia may develop. It may be due to a localized peritonitis. Pyrexia independent of local causes is seldom pronounced until the stage of cachexia, when from time to time an afternoon temperature of 102° may be registered. The fever is similar to that which is present in leukæmia and all grave anæmiæ. No satisfactory explanation has ever been given for its occurrence.

Circulatory Symptoms. The heart may be slightly dilated; hæmic murmurs are often heard, especially in the later stages. The carotids and other large arteries throb visibly, and a capillary pulse is not infrequently noted. The pulse is full and frequent, and may approach the water-hammer character. The veins are often prominent, and the bruit de diable may be heard in the neck.

Pulmonary Symptoms. Râles due to compression of the lung by the splenic tumor are often present at the base of the left lung. Dyspnœa, due to deficient hæmoglobin and the elevation of the diaphragm, is experienced.

Digestion. As a rule, the appetite is fair until the disease is well advanced, when it gradually fails. Nausea and vomiting may be early symptoms, and when associated with paroxysms of pain in the region of the spleen may cause much distress. The gastric disturbances may be due to pressure, or, possibly, may be reflex through involvement of the sympathetic nervous system. Diarrhœa may be an early symptom and persist for several weeks or months. Constipation often alternates with diarrhœa. Toward the end diarrhœa may be incoercible, and at last involuntary evacuations may take place. Hemorrhage from the stomach has been recorded.

Nervous System. The symptoms referable to the nervous system are those chiefly of anæmia—namely, vertigo, headache, neuralgia, and mental fatigue. The mind usually remains clear until near the end.

Blood. The blood varies with the stage of the disease. In the beginning of the affection there is only a slight reduction in the number of red blood-corpuscles and a relatively greater diminution in the hæmoglobin. After the disease is well advanced the blood is very pale and thin. Its coagulability is very much reduced. Red blood-corpuscles: The red blood-corpuscles are, as a rule, very much diminished in number. In the few cases in which they have been counted the results have ranged from about 4,000,000 to 568,000 per c.mm.; the average case will show about 2,500,000 per c.mm. at the beginning of the stage of cachexia, and as the disease progresses the number usually decreases. There is no marked alteration in the form and size of the corpuscles. Poikilocytosis has not been recorded. The corpuscles are pale. Nucleated red blood-corpuscles have not been observed. Roleaux formation is absent in the later stages. The hæmoglobin is reduced in quantity; the individual corpuscle contains less hæmoglobin than normal. The color index, however, does not seem to be as low as in chlorosis. In my case, although the hæmoglobin was reduced to 10 per cent., the color index was never lower than about 0.85. White blood-corpuscles: In the majority of cases the leucocytes are normal in number, and the relation of the different forms is not disturbed. No abnormal elements have been recorded. In one of Banti's cases the number was increased to 19,805 per c.mm., but in this case pneumonia was present as a complication. In Franzolini's case five times the normal number were found. Under such circumstances the character of the leucocytes alone would enable one to differentiate the disease from splenic leukæmia.

Urine. The urine is normal in quantity and may not show special changes. A large quantity of nucleohistone was found by Stein in a clinical case of splenic pseudoleukæmia. The solids of the urine are not altered in a characteristic manner. A trace of albumin has been found. Signs of extensive degenerative changes in the kidney have not been observed; sugar is absent. I was able to produce alimentary glycosuria by administering a moderate quantity of glucose. This was due, no doubt, to impairment of the function of the liver.

DIAGNOSIS. Essential to the diagnosis of splenic pseudoleukæmia is (1) an idiopathic splenic hypertrophy; (2) a progressive anæmia without a leucocytosis presenting the characteristics found in leukæmia; (3) the absence of marked lymphatic enlargement. Since neither signs of anæmia nor local sensations have been noted previous to the development of splenic hypertrophy, the disease could scarcely be suspected before the spleen was palpable. In relation to splenic hypertrophy, one must determine whether the palpable structure in the left hypochondriac region is a splenic tumor, and, if so, its nature. As a rule, tumors of the spleen present less difficulty in diagnosis than those of any other abdominal structure. They emerge from beneath the left costal arch and cling closely to the abdominal wall, overriding all structures in the abdominal cavity. Their development is downward, along a line which is directed toward the right pubic bone.

Splenic enlargements are respiratory movable, and in a diagonal direction, which is peculiar to splenic tumors. All other structures attached to the diaphragm have a tendency to move in a line parallel with the long axis of the body. A variable degree of lateral motion is permitted. The structure is uniform in consistency, outline, and surface, which constitutes a true hyperplasia in the clinical sense. Unless the spleen is dislocated it is impossible to grasp its upper margin, but the palpating finger rests on a smooth surface, which seems to be a part of a structure which extends upward beneath the costal arch. Its inner and lower margins are readily palpated, and the lower pole may often be grasped, which is characteristic of splenic enlargements. The inner margin is notched. The dulness on percussion over the structure in the abdominal region is continuous with that of a uniform dulness in the splenic region, extending often to the eighth rib in the post-axillary and the sixth rib in the anterior axillary line.

Tumors of the kidney are usually fixed, and their development from the lumbar region is evident on bimanual palpation. They develop, as a rule, downward, and, unless extremely large, seldom encroach upon the diaphragm. Urinary symptoms are often present, and the colon may be demonstrated as lying in front of the kidney mass.

Enlargement of the left lobe of the liver may present some difficulty in diagnosis. Under such circumstances the direction of the respiratory mobility, and, above all, the continuity of its lower border with the lower border of the liver in the epigastric region, would serve as distinguishing features. Having determined that the mass in the left hypochondriac region is a splenic structure, the nature of the enlargement must next be considered. It is characteristic of splenic hyperplasia that the form and outline of the normal spleen is retained. A neoplasm, such as carcinoma of the spleen, is to be excluded, or at least can scarcely be diagnosed in the absence of irregularities in the structure. Acquired syphilis rarely produces great enlargement of the spleen in the early stages of the disease, and still more rarely as a tertiary manifestation, excepting when combined with amyloid degeneration. The history, presence of amyloid elsewhere, and other signs of syphilis would render the diagnosis easy.

Enlargement of the spleen from tuberculosis would rarely present any difficulty in diagnosis. Echinococcus of the spleen is to be distinguished by its long course without general symptoms and the presence of fluctuation. In case of doubt, puncture would clear up the diagnosis. After having excluded all forms of neoplasm and cyst a hyperplasia of the spleen may be assumed. Its nature would then require careful consideration. A differential diagnosis should be made between the morbid states which are accompanied by a splenic hyperplasia, namely, leukæmia, malarial cachexia, passive congestion, progressive pernicious anæmia, amyloid spleen, and Banti's splenomegalia with hepatic cirrhosis.

Splenic Leukæmia. The clinical phenomena are so nearly identical in the two affections that a blood examination shows the only essential difference between them. A slight increase in the polynuclear variety of leucocytes may be present in splenic pseudoleukæmia. In one of Banti's cases there was an absolute leucocytosis, but the blood examination was not made until the day upon which a pneumonia developed. In this and in a few other cases in which a moderate leucocytosis has been present the quality of leucocytosis has not been accurately stated. In the diagnosis of leukæmia, when leucocytosis is only moderate, the quality of the leucocytes, not their number, determines the diagnosis. Essential to the diagnosis of leukæmia with moderate leucocytosis is the increase in the mononuclear elements, which often show degenerative changes in their nuclei. As a rule, in splenic pseudoleukæmia there is a normal number of leucocytes, and the relation of the different forms is not disturbed. The number of red blood-corpuscles is at first moderately reduced. Later in the disease the number may be diminished to two million or one million, or, as in my case, to a little more than half a million per cubic millimetre. Change in size and form of the red blood-corpuscles is not marked. The individual red blood-corpuscles are poor in hæmoglobin and rarely contain nuclei. A more extended account of the blood in splenic pseudoleukæmia is to be found under symptomatology. The differential diagnosis between the clinical pictures presented by splenic pseudoleukæmia and splenic leukæmia is to be made only by a study of the white blood-corpuscles.

Malarial Cachexia. The form of malaria known as malarial cachexia, characterized by enlargement of the spleen and anæmia, presents clinical phenomena very closely simulating splenic pseudoleukæmia. Splenic hypertrophy, enlargement of the liver, and anæmic cachexia are essentially the same in both affections. Indeed, it must be admitted that a positive differential diagnosis between the two conditions could not be made under certain circumstances; as a rule, however, the differential features are sufficiently prominent to leave no doubt as to diagnosis. In all cases so far reported which are to be included in the category of splenic pseudoleukæmia, malaria has been carefully excluded as an etiological factor. A malarial cachexia, developing, as it sometimes does, in intense malarial districts, without chills, would present features requiring great care in diagnosis. In doubtful cases the presence of the plasmodium in the blood would, of course, be conclusive evidence as to the nature of the disease. Blood-pigment in the white blood-corpuscles, or free in the plasma, has not yet been noted in quantities approaching that found in malarial cachexia. The pigmented skin is a slate or dirty yellow color, peculiar to chronic malaria. In splenic pseudoleukæmia pallor is combined with subicterus. In districts where malaria is intense a nephritis not infrequently complicates the disease, while it has never been noted in cases of splenic pseudoleukæmia. Inhabitants of a malarial district who have never had the usual manifestations of malaria, as well as those who unquestionably have suffered from the disease, may develop splenic hypertrophy, which often persists for a long time, even a period of years, without the appearance of anæmic cachexia or serious disturbance in general health. Splenic pseudoleukæmia is characterized by a splenic hypertrophy which is directly associated with or very soon followed by a progressive anæmia, which invariably continues to cachexia, with fatal termination in a definite period of time unless the disease is arrested. The therapy which in time will relieve a malarial cachexia has no particular effect on splenic pseudoleukæmia.

Essential Anæmia. In *chlorosis* the blood findings and clinical phenomena of the early course of the disease may be very similar to those of splenic pseudoleukæmia. However, in chlorosis the splenic enlargement is absent or seldom marked, and when present follows rather than precedes the development of the anæmia. The course and effect of treatment in the two affections is entirely different.

In *primary progressive pernicious anæmia* the cachexia, course, and clinical phenomena resemble the manifestations of this disease in many particulars, but the blood findings and splenic hypertrophy present differences sufficiently great to establish the diagnosis. In primary progressive pernicious anæmia the individual corpuscle is relatively rich in hæmoglobin, while in pseudoleukæmia it is poor. There is a much greater difference in the size and form of the red blood-corpuscles in primary progressive pernicious anæmia. Nucleated red blood-corpuscles are rarely, if ever, found in splenic pseudoleukæmia, while they are constantly found in primary progressive pernicious anæmia. The large form of nucleated red blood-corpuscle—the gigantoblast—of special importance in the diagnosis of primary progressive pernicious anæmia, has never been found in splenic pseudoleukæmia. In primary progressive pernicious anæmia the spleen is more often atrophied than enlarged. The enlargement, if sufficient to be detected on palpation, is never great, usually shows fluctuation in size under treatment, and always follows the development of anæmia. Mosler and Gast believe the enlargement of the spleen in chlorosis and primary progressive anæmia to be a compensatory hypertrophy directly connected with the regeneration of the blood. Other authors, as Immermann, Eichhorst, Müller, and Neumann, do not believe that under such circumstances the spleen returns to its prenatal hæmotopoitic function. By others the splenic enlargement in the anæmiæ is thought to be due to the increased destruction of red blood-corpuscles. The liver is nearly always hypertrophied in splenic pseudoleukæmia. In primary progressive pernicious anæmia it is not.

Passive Congestion of the Spleen. In this condition the etiological factors of a liver cirrhosis or other conditions inducing splenic hyperæmia would nearly always be evident. The course of the two diseases is somewhat different. The development of anastomoses between the portal and general circulation, and the other signs of liver cirrhosis, such as early appearance of ascites and late appearance of cachexia, characterize the spleen of passive congestion. The enlargement of the spleen in passive congestion is moderate in comparison to the enormous hypertrophy sometimes present in splenic pseudoleukæmia. In atrophic cirrhosis the liver is small, while in splenic pseudoleukæmia it is hypertrophied. On the other hand, cirrhosis of the liver accompanied by marked fatty infiltration and enlargement of the organ presents clinical features which under certain circumstances might give rise to great difficulty in diagnosis.

Amyloid Spleen. The diagnosis of amyloid spleen is to be made only when a sufficient cause has preceded its development, such as long-continued suppuration of bone or soft parts, phthisis pulmonum, or protracted syphilis. Evidence of amyloid degeneration elsewhere is to be desired in connection with its etiology. Although the spleen is usually the first organ to show amyloid changes, the diagnosis of amyloid spleen without signs of amyloid liver, kidneys, or intestines would be at best a probable diagnosis.

Splenomegalia with Cirrhosis of the Liver. Banti[1] describes a condition characterized by splenic hypertrophy associated with cirrhosis of the liver, in which he believes the primary disease is of the spleen, and that the cirrhosis of the liver results from the pathological changes in the spleen. The clinical difference between the affections is so slight that Banti admits that on that alone no distinction between the two affections can be made.

The diagnosis of splenic pseudoleukæmia is often surrounded by many difficulties. In all cases the evidence must be accurately obtained and the proper valuation placed on it to ensure trustworthy results. Undoubtedly, there are cases in which it would be advisable to withhold a positive diagnosis for a variable period of time.

COURSE AND PROGNOSIS. The disease presents a definite course within certain limits of variation. Its tendency is distinctly progressive. The severity of symptoms may show slight remissions; but, on the whole, it will be observed that the patient loses ground rather steadily from month to month. It is difficult to estimate the exact duration of the disease, owing to the uncertainty of the length of the first stage. In some cases a fatal termination has been reached in five or six months after the first symptoms were manifest. The average duration appears to be about two years. My case terminated in about three and a half years from the time the splenic enlargement was first noticed. That duration seems to be about the longest recorded. While the first and second stages of the disease may vary and be prolonged for a period of one or more years, the cachectic stage seldom continues more than a few weeks or five or six months. Death results from progressive marasmus and intercurrent disease. Medical treatment seems to be of no positive value in controlling the progress of the disease. The removal of the spleen has arrested the process in the cases noted in the chapter on treatment. The prognosis is decidedly unfavorable without surgical intervention.

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[1] Semaine Med., 1894, xiv. 318, and Ziegler's Beitrage, 1898.

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REVIEWS.

THE MEDICAL COMPLICATIONS, ACCIDENTS, AND SEQUELÆ OF TYPHOID OR ENTERIC FEVER. By HOBART AMORY HARE, M.D., B.Sc., Professor of Therapeutics in the Jefferson Medical College of Philadelphia, etc., with a Special Chapter on the Mental Disturbances following Typhoid Fever, by F. X. DERCUM, M.D., Clinical Professor of Diseases of the Nervous System in the Jefferson Medical College. Philadelphia and New York: Lea Brothers & Co., 1899.

CAN anything new be said about typhoid fever, a disease so widespread, so carefully observed, so critically studied, so voluminously written about, that knowledge concerning it would seem to be wellnigh complete and additional literature superfluous? Can even the industrious Hare glean from his own rich experience or that of others aught that is fresh concerning the medical complications of this preventable, disgraceful, filth disease? One must answer both no and yes. The facts concerning the atypical clinical manifestations of the affection, the numerous statistics, are largely gathered from authors who are dead or whose works are already well known. Louis, Fagge, Murchison, Liebermeister, Wunderlich, Immermann, Osler, and Fitz are men whose writings on typhoid are classic, though in some instances of recent date. There is, we might say, nothing new in this respect. But, on the other hand, there is much that is new unless one has kept in closest touch with the most recent literature. It is not so much, perhaps, the new fact that is of importance as it is the new point of view from which a fact is observed. Bacteriology has completely modified our conception of the disease. In its light even those dry old statistics have a glow of life. Instruments of precision and improved technique have made diagnosis surer. The Widal test, the Ehrlich reaction, the examination of the blood for leucocytosis or for bacilli clears up many a doubtful diagnosis. Pneumonia, cystitis, meningitis, cholecystitis, etc., long viewed as accidental or intercurrent affections, wear an entirely new aspect when viewed as localized manifestations of the working of the specific organism. Typho-malarial fever is banished or rightly looked upon as a double infection, typhoid and malaria; apyretic, mild, and abortive cases are more easily recognized, and cases that might escape the notice even of the morbid anatomist, because of absence of intestinal lesions, are made clear by the bacteriological test. It is, after all, the same old disease of Louis and Murchison and Liebermeister, with the same complications, but yet completely changed, because we have changed our point of view, even admitting that there have been some modifications in type as compared with the disease of the preceding generation, due to improved therapy and acquired relative immunity. To one who is not fully alive to the newer conception of typhoid, Hare's book is of the greatest value, for it treats of the subject in the light of the most recent knowledge.